the use of e-health interventions.*Both B. F. M. Wijnen and L. A. M. Leenen contributed equally to this work.

PRM226
IMPLEMENTATION OF INTERNATIONAL CHART REVIEW STUDIES: AN ASSESSMENT OF ETHICS AND REGULATORY CONSIDERATIONS
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OBJECTIVES: In the absence of secondary sources of health care data, chart review studies can result in patient level data repositories including patient characteristics, care patterns, treatment effectiveness and clinical and safety outcomes. Data can be used to populate economic evaluations, and value dossiers, and inform drug safety assessments. For successful implementation, however, knowledge of country-specific ethics and regulatory approval processes is paramount. **METHODS:** Operational, ethics and regulatory issues and considerations as well as strategies for study success have been summarized in the context of eleven recent multi-national chart review case studies. **RESULTS:** Two of 11 studies also collected data prospectively; two studies were categorized as post authorization safety studies and three studies were conducted in peri-approval compassionate use program populations. The majority of studies (9) were oncology focused, with two studies focused on infectious diseases and opioid-induced constipation. Sample sizes varied from 20 to 500 patients, the number of countries from 1 to 8, and the number of sites from 4 to 61. All studies included at least one European country. Across studies, key operational considerations that impacted the ethical/regulatory approval process were ambiguous/amorphous multinational regulatory requirements/guidelines; commercial availability or non-availability of the sponsor product at the time of chart abstraction; data collection method(s) (i.e., retrospective vs. hybrid chart review plus prospective data collection); country variation in informed consent requirements and definitions of personal data; and multinational contractual requirements with the participating sites. **CONCLUSIONS:** International chart review studies are an effective methodology to resolve data gaps not solved by existing secondary health care data sources resulting in tailored, patient-level datasets. Current knowledge of the highly variable and evolving global regulatory requirements, as well as the development of a risk management plan informed by methodological and operational lessons learned at study-outset will facilitate risk mitigation and allow researchers to overcome key challenges.

PRM227
COST PER PATIENT IN NON INTERVENTIONAL STUDIES AND ADDED VALUE OF DIRECT TO PATIENT CONTACT SERVICE
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OBJECTIVES: In addition to study outcome concerns arising from patients lost to follow-up (LFU) in pharmacoepidemiology and pharmacovigilance studies, the financial impact of LFU can be significant. Our objectives were to estimate cost per patient in Non-interventional studies, to identify variables that may affect this patient cost, to estimate cost of patient lost to follow-up (LFU), and financial benefits that can be expected from LFU minimization through Direct to Patient Contact service (DPC). **METHODS:** Analysis of 2013 proposals and budgets submitted to study sponsors. Selection criteria: non interventional, prospective, longitudinal patient follow-up, full CRO services. Analysis were performed according to patient sample size, study duration, disease category, and different hypothesis for LFU rates. **RESULTS:** 1) 20 studies (Domestic, Regional or Global) met all inclusion criteria; 2) Annual cost per patient -ranging from €1,068 to €4,370- decreases as the study duration increases (set-up cost is more diluted in the patient annual cost). But the longer the study is the more expensive the overall cost per patient; 3) Mean annual patient cost significantly differs according to rarity of disease/population; rarity is an important criterion that greatly impacts overall and annual patient cost, especially for study lasting more than 1 year. Below 1 year, the cost per patient remains quite similar between types of diseases/populations; 4) Cost are more significant in rare diseases studies, therefore DPC can provide the best overall cost savings in these populations; and 50 The cost savings are depended on the expected rate of patient LFU-with/without DPC service and the planned patient sample size. **CONCLUSIONS:** Return On Investment plays an important role for Sponsors to determine if DPC is valuable in a study. The financial investment may be beneficial regardless of the cost to insure completion of the patients, thus meeting the scientific study objectives. But it could generate cost savings as well.

PRM228
RETROSPECTIVE CHART REVIEW STUDIES: STRATEGIES TO ENSURE ROBUST DATA QUALITY
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OBJECTIVES: Retrospective chart review studies can result in robust naturalistic data to inform evaluations of treatment patterns, resource utilization, costs of care, clinical outcomes and safety. Data quality control is challenging both as a result of poor quality documentation in the usual care medical chart, or as a result of data abstraction and data entry processes. **METHODS:** Ten chart review case studies conducted in the United States, Canada and Europe were evaluated to provide recommendations for improving chart review data quality control mechanisms. **RESULTS:** All 10 studies used electronic data capture (EDC) systems. Common lessons learned across the studies were that the case report forms (CRFs) should only include necessary data points required to fulfill the analysis. Direct chart-to-EDC data entry and remote real-time data quality control is recommended to reduce additional transcription errors that may occur if using paper CRFs. It is important to ensure the EDC system includes a cohort-control platform that enables selection of patient cohorts (i.e., random selection) and tracking of eligibility screening to reduce selection bias risk. Automated edit checks of primary data endpoints should be programmed into the EDC system prompting data abstractors to revise erroneous data and/or confirm data outside of expected ranges at entry. To confirm abstracted data reflect source documents (patient medical charts), a second abstractor at the site can re-abstract pre-defined critical study variables from patient medical charts for cross-referencing for data discrepancies. Site training must be effective to ensure compliance with chart abstraction and data quality requirements. **CONCLUSIONS:** Given the frequent incomplete or poor quality medical chart information and the potential for human error in data abstraction and entry processes, data quality control methods are paramount. Approaches to protocol, CRF and study training materials design can positively impact data quality.

RESEARCH ON METHODS – Conceptual Papers

PRM229
RESEARCH PRIORITIZATION IN AN MCDA CONTEXT: EXISTING METHODS - NEW RESULTS
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OBJECTIVES: Health technology assessment typically involves consideration of multiple conflicting criteria. Therefore, trade-offs are required between different objectives such as maximizing health, restricting budget impact, increasing health equity and maximizing safety. Methods such as multiple decision criteria analysis (MCDA) are therefore increasingly being used to reflect such trade-offs in a transparent and consistent manner. Although MCDA can be combined with cost-effectiveness analysis it may, however, invalidate results from Value of Information (VOI) analysis when it also includes other health-related or cost-related objectives. **METHODS:** In two case studies we first applied VOI methods directly and only to cost-effectiveness estimates, and then also applied these methods separately to all relevant decision criteria. In a simulation study on two drugs we calculated the expected value of perfect information (EVPI) with drug selection concerning a trade-off between cost-effectiveness and drug safety. In a clinical study on the primary prevention of cardiovascular disease using improved versus standard risk prediction we calculated the EVPI with selection of the best risk prediction strategy concerning a trade-off between cost-effectiveness and budget impact. **RESULTS:** In our simulation study we found EVPI estimates per patient based only on cost-effectiveness were up to € -586 lower and € +459 higher compared to EVPI estimates also acknowledging the safety criterion, depending on its weight. In our clinical study, the EVPI estimates based only on cost-effectiveness were consistently lower, up to € -540 per patient, compared to EVPI estimates also acknowledging the budget impact criterion. **CONCLUSIONS:** When decisions are based not only on cost-effectiveness but on other criteria as well, some of which also relate to costs or health effects, standard VOI estimates are no longer valid. However, separate application of VOI methods to each of the relevant decision criteria is straightforward and can facilitate transparent research prioritization in a complex MCDA context.

PRM230
A STATISTICAL MODELING FRAMEWORK TO CHARACTERIZE THE IMPACT OF PROGRESSION ON SURVIVAL IN ONCOLOGY
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The benefits and value of new cancer treatments often focus on the overall survival (OS) gains that patients may derive. Trials are typically not long enough to allow detailed understanding of OS, and potential benefits must be inferred from benefits on progression-free-survival (PFS). This raises questions such as whether early or later progression impacts survival, whether the increase in mortality following progression is sustained or gradually diffused, and whether a benefit observed on PFS implies a benefit in OS. Answering these questions requires an analytical framework in which progression and survival can be analyzed together and parameterized to address key questions. We propose a statistical modeling framework based on Cox regression and time-dependent predictors and effects. A simple formulation of this model would include a time-dependent indicator for progression, whose coefficient would measure the increase in risk of death following the event. This is very limiting, however; it assumes that the timing of progression does not matter and that the increase in risk of death is sustained indefinitely. A more flexible formulation can be built using two descriptors of event: the timing of progression (TP) and time since progression (TSP). These can be continuous measures or categorized (e.g., early vs. late TP), as appropriate. The coefficient for TP reveals whether later progression is associated with higher/lower subsequent mortality, while the coefficient of TSP reflects whether and for how long the increase/decrease in mortality is sustained and whether it ever returns to the level of patients who had not progressed. The impact of treatment can be captured on each of these parameters separately. The proposed framework will be illustrated with an example, and extension of the approach to other applications (e.g., measuring the impact of a stroke on survival) will be discussed.

PRM231
TOWARDS INTEGRATION OF RESEARCH EVIDENCE ON PATIENT PREFERENCES IN COVERAGE DECISIONS AND CLINICAL PRACTICE GUIDELINES: A PROPOSAL FOR A TAXONOMY OF PREFERENCE-RELATED TERMS
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Despite the availability of a large body of research evidence on patient preferences for health outcomes and/or health care services, its use in health care policy decisions is limited. This contrasts with the current increasing attention for patient-cen-